Notice of Allowability	Application No.	Applicant(s)	
	10/613,639	MONTGOMERY, ALAN BRUCE	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *9/25/06*.

2. ☒ The allowed claim(s) is/are *12, 29-33, 21-23, 25-27, 13-15, and 24 [renumbered as 1-16]*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *20061220& 20061221* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Hana Verny, J. D. on December 20, 2006 at 3:30 pm EST and on December 21, 2006 at ~7:00 pm EST.

The application has been amended as follows:

(1) On page 1, line 5 of the specification after the number "2001" insert, "(now U.S. Patent No. 6,660,249)".

(2) In claim 25, line 2 and claim 29, line 2 delete the word "salt".

(3) In claim 14, line 3, insert "w/v," after the comma following the word "chloride".

(4) Rewrite claims 12, 13, 15, 21-24, and 27 as indicated below:

12. (Twice amended) An inhalable composition comprising ~~from about 1 to about 250 mg of~~ aztreonam lysinate ~~salt per one dose~~, said composition suitable for the treatment of pulmonary bacterial infections caused by gram-negative bacteria, wherein said aztreonam lysinate is

prepared as an inhalable dry powder having a particle size with a mass medium average diameter from about 1 to about 5 μ.

13. (Twice amended) The composition of claim 25 wherein said aztreonam lysinate ~~salt~~ is ~~dissolved into~~ in a solution comprising a volume of saline from about 1 to about 5 ml ~~of saline~~, said saline comprising between about 0.09% and about 0.9% of chloride, w/v, or an equivalent amount of bromine or iodine, wherein said solution is aerosolable and wherein said aerosolable solution has a pH from about 4.2 to about 7.5.

15. (Twice amended) The composition of claim 14 wherein ~~said saline and~~ the aztreonam lysinate ~~salt are formulated separately for reconstitution of the aztreonam lysinate dry powder for aerosol wherein the dose of aztreonam lysinate~~ is present in a concentration of about 75 mg/ml in said saline ~~diluent~~.

21. (Currently amended) The composition of claim ~~13~~ 12 comprising from about 1 to 250 mg of the aztreonam lysinate, wherein the composition may be administered as the inhalable dry powder by a dry powder inhaler or~~,~~ as a diluted saline solution by a metered dose inhaler ~~or as the aerosolable solution~~.

22. (Twice amended) The composition of claim 21, comprising 10 to 100 mg of aztreonam lysinate ~~administered in a dose from about 10 to about 200 mg of the aztreonam lysinate salt twice a day~~.

23. (Twice amended) The composition of claim 22 comprising 75 mg of aztreonam lysinate ~~salt~~, wherein said composition may be administered twice or three times a day.

24. (Twice amended) A method for administering aztreonam lysinate ~~The composition of claim 21~~ comprising administration of the composition of claim 21 by a dry powder inhaler or by a metered dose inhaler, wherein said composition may be administered one to twelve times a day, provided that if the composition is delivered more than ~~then~~ twice a day, a total dose of aztreonam lysinate ~~salt~~ is not higher than 750 mg a day.

27. (Twice amended) The composition of claim 26 wherein said alpha aztreonam lysinate ~~salt~~ contains less than 100 ppm of residual alcohol and ~~ethyl alcohol residue~~ initial levels of contaminants generated from the alpha aztreonam lysinate are less than ~~0.1 and~~ 1%.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: claims 12-15 and 21-33 were found allowable based upon Applicants' persuasive arguments and the above Examiner's amendments, because the prior art does not teach, suggest, or motivate one of ordinary skill in the art to obtain an inhalable composition of aztreonam lysinate having a mass medium average diameter from about 1 to about 5 microns. Specifically, the Kuo reference does not provide a motivation for a person of ordinary skill in the art to select aztreonam as the active agent from a list of 100+ active agents (see col. 6, line 52 through col. 7, line 51) or a specific salt of aztreonam for use in Kuo's invented compositions, because (1) inhalable dry powders

comprising aztreonam are not exemplified and (2) no specific salt of aztreonam is taught by Kuo. Bastin does not cure the deficiencies of Kuo; because it only provides a general teaching of pharmaceutically acceptable salts often utilized in the development of pharmaceutical compositions and suggest that lysinate salts are interchangeable with arginate salts.

Regarding aztreonam amino acid salts, injectable forms of aztreonam, wherein aztreonam is used as the arginate salt (Varia et al. EP 0297580; IDS), are known in the prior art. It has been recognized in the prior art that arginine is not suitable for inhalation (Pediatrics 1975, 55(1), 96-100; provided with this notice of allowance). The prior art has also recognized that the commercially available aztreonam arginate salt (AZACTAM®) is not suitable for inhalation and is not approved for inhalation administration (Montgomery, U.S. Patent No. 6,660,249 col. 8, lines 7-58). Inhalation of aztreonam arginate was reported to cause bronchospasm in one of nineteen cystic fibrosis patients involved in a clinical study utilizing aztreonam arginate to treat pulmonary infections (Spanish Annals of Medicine, 1994, 40(3); IDS). Prior to treatment by administration of a nebulized solution of aztreonam arginate required the administration of bronchodilators and respiratory physical therapy (Spanish Annals of Medicine, 1994, 40(3), 2nd page, right hand column). Therefore, it would not have been obvious to a person of ordinary skill in the art to modify injectable formulations of aztreonam arginate for inhalation or to select the lysinate salt as a suitable alternative to the argininate salt.

The terminal disclaimer filed on September 25, 2006 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of U.S. Patent No. 7,138,419 and allowed copending application 10/654,815 has been reviewed and is accepted. The terminal disclaimer has been recorded and the obviousness-type double patenting

rejections over copending applications 10/882,985 (now U.S. Patent No. 7,138,419) and 10/654,815 (this application was allowed on December 7, 2006, but has not been assigned a U.S. patent number) are now moot.

Regarding the Examiner's amendment to claim 12, Applicants have support for the bulk aztreonam lysinate dry powder with mass medium average diameter from about 1 to about 5 μ at least in Example 3 (pg. 66, line 25 through pg. 67, line 20), Example 5 (pg. 69, line 30 through pg. 70, line 9), Example 6 (pg. 70, lines 10-31), and on pg. 10, lines 11-18.

Concerning the Examiner's amendment to claim 24, support for the method is found at least on pages 33-35.

The Examiner's amendment to claim 27 to the second line of said claim has support found on page 21, lines 25-30 of the instant specification.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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